

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Andrew VAILLANT et al.  
Serial Number: 10/661,097  
Filing Date: September 12, 2003  
For: ANTIVIRAL OLIGONUCLEOTIDES TARGETING HSV AND CMV  
Art Unit: 1648  
Examiner: Jane J., Zara  
Agent: Cawthorn, Christian

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**DECLARATION UNDER 37 C.F.R. SEC. 1.132**

I, Jean-Marc Juteau, do hereby declare and state as follows:

1. I received the degrees of Bachelor (B.Sc.) of Biology from Montreal University in 1985, Master (M.Sc.) of Microbiology and Immunology from Montreal University in 1988, and Doctor of Philosophy (Ph.D.) of Microbiology and Immunology from Laval University in 1991.
2. My academic background and experiences in the field of the present invention are listed on the enclosed *curriculum vitae*.
3. I am a founder since 1999 of REPLICor Inc. and Senior Vice President since 2002.
4. I am an author of several scholarly publications as listed in my enclosed *curriculum vitae*.
5. I am an inventor in the present application; I have read and am thoroughly familiar with the contents of U.S. Patent Application Serial No. 10/661,097 entitled

“ANTIVIRAL OLIGONUCLEOTIDES TARGETING HSV AND CMV”, including the claims.

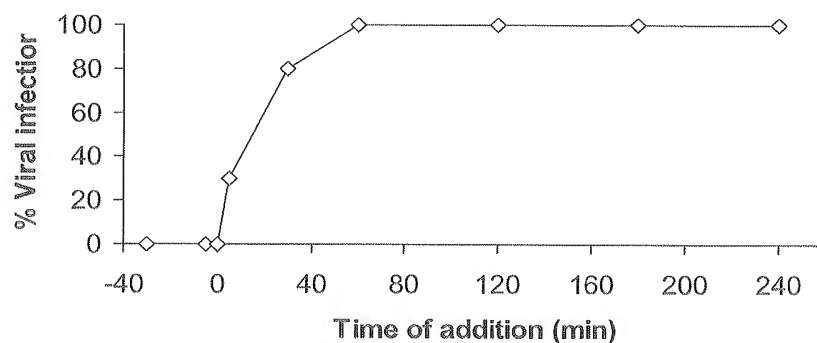
6. I have also read and understood the latest Official Action from the PTO dated March 6, 2008. In this Office Action, claims 1, 2, 14, 15, 17, 18, 21, 22, 27-29 and 39 have been rejected under 35 U.S.C. 112, first paragraph. In addition, claims 1, 2, 14, 15, 17, 18, 21, 22, 27-29, 39 and 42 have been rejected for allegedly being obvious in view of the teaching found in Sundquist et al., and in view of Trus et al. and McKay et al.
7. The following experiments had been performed between years 2003 and 2007 by scientific collaborators under the supervision of Andrew Vaillant (inventor on this invention) and myself. In order to determine the mode of action of oligonucleotides (ONs) described in this invention in herpesviridae, we tested ONs for activity against several representatives of this family, including HSV-1, HSV-2 and cytomegalovirus (CMV). The mechanism of action of these ONs in two herpesviridae may be applied to other members of this family since all herpesviridae have generally conserved adsorption (attachment, binding) and infection (entry) mechanisms. Moreover, we have shown that all herpesviridae are susceptible to these ONs. **This data clearly differ from Sundquist et al. (20050009743) which describes sequence dependent activity of (TG)<sub>n</sub> ON on promoting the assembly of capsid-nucleocapsid.**

#### **Mode of action of ONs in HSV-1**

*Method:* Plaque reduction assay. VERO cells were grown to confluence in 24 well tissue culture plates. Upon reaching confluence, the media was changed to contain 5% FBS and inoculated with HSV-1 (strain KOS, 40-60 PFU total). Viral adsorption proceeded for 90 minutes, after which cells were washed and replaced with new "overlay" media containing 2% FBS and 1% human immunoglobulins. Three to four

days after adsorption plaques were counted following formalin fixation and crystal violet staining. IC<sub>50</sub> values were calculated as the concentration of compound which reduced the number of plaques by 50% compared to the untreated control.

*Results:* To determine where in the replicative cycle ONs were exerting their anti-herpetic activity, we performed a time of addition study using the plaque reduction assay in HSV-1. For these experiments we used REP 2006 at a concentration of 1  $\mu$ M which is greater than the IC<sub>99</sub> for this PS-ON in the plaque reduction assay. When added either before or during viral infection, the ON was fully effective in preventing HSV-1 activity, however it rapidly lost its ability to inhibit viral activity when added at increasingly longer times after infection (see figure below) and had no effect when added 60 minutes or later after infection on viral activity. These observations suggest that ONs act at least during the adsorption (binding) and at least on infection (entry) of HSV-1 into the host cell.



#### **Mode of action of ONs in HSV-2**

*Method:* Synchronized infection /kinetic assays. CaSki cells, on 12 well plates, were cooled to 4°C and inoculated with ~200 to 300 PFU of virus/well at 4°C for 4 h, a temperature permissive for viral binding (adsorption), but not entry (infection).

Unbound virus was removed by washing the cells 3 times and the cultures were then shifted to 37°C for 30 minutes to permit viral infection. Plaques were counted by immunoassay (black-plaque). ONs were added either during the 4° C binding period or at the time of temperature shift (entry).

*Results:* To determine which steps in HSV-2 infection were blocked by ONs, their activity when added during adsorption or entry were compared in a synchronized infection assay. HSV binding, which occurs at 4°C, can be experimentally differentiated from entry, which occurs after a temperature shift to 37°C. ONs were added at the time of binding (for 4 hours at 4°C) or entry (for 30 minutes at the time of temperature shift to 37°C). Heparin, a competitive inhibitor of HSV binding served as a control. Heparin significantly inhibited HSV plaque formation if present during binding but had little effect if added at entry. REP 2006 and REP 2031 behaved similarly and completely inhibited HSV-2 infection if added during binding or inhibited ~ 50% of viral infection if present during the immediate temperature shift (entry) (see table below). These observations suggest that ONs can act at least during the adsorption (binding) and infection (entry) of HSV-2 into the host cell.

	No drug	Heparin (100ug/ml)	REP 2006 (10uM)	REP 2031 (10uM)
Drug added during binding	196	0	0	0
Drug added during viral entry	195	150	104	97

Numbers indicate plaque counts

### **Sequence independent activity of ONs in herpesviridae.**

The following tables recapitulate the *in vitro* and *in vivo* activity of several ONs described in this invention among different members of herpesviridae. This data demonstrates that ONs have a **sequence independent mode of action and are active throughout the herpesviridae family.**

#### Activity of different size ONs randomer in HSV and CMV

<b>Randomer PS-ON size (bases)</b>	<b>In vitro HSV-1 activity (uM)</b>	<b>In vitro HSV-2 activity (uM)</b>	<b>In vitro CMV activity (uM)</b>
6	>1	Not tested	Not tested
10	>1	Not tested	Not tested
20	0.44	0.86	4.42
30	0.115	0.14	0.85
40 (REP 2006)	0.079	0.012	0.13
50	0.053	Not tested	Not tested
80	Not tested	Not tested	0.19

#### Activity of different ONs HSV is sequence independent

<b>PS- ON Sequence</b>	<b>HSV-1 (IC50 uM)</b>
40 mer poly C (REP 2031)	0.097
40 mer poly G	No activity
40 mer poly T	0.19
40 mer poly A	0.614
40 mer poly AC	0.123
40 mer poly TC	0.199
40 mer poly AG	0.098

### Activity of ONs in herpesviridae

Virus	Strain	EC50 ( $\mu$ M)				
		REP 2006	CDV	ACV	FOS	GCV
HSV-1	KOS <sup>a</sup>	0.14 +/- 0.022	- <sup>b</sup>	3.2	163.7	-
	E-377 <sup>c</sup>	0.2	-	1.3	-	-
HSV-2	MS2 <sup>a</sup>	0.06 +/- 0.013	-	2.8	51.7	-
	MS <sup>c</sup>	0.02	-	0.4	-	-
CMV	AD169 <sup>a</sup>	0.13 +/- 0.016	1.61	-	59.4	5.9
	HCMV	0.02	-	-	-	3.9
VZV	Ellen <sup>c</sup>	<0.02 (n=2)	-	0.1	-	-
EBV	P3H-R <sup>d</sup>	14.7 +/- 3.7	-	6.4 +/- 5.9	-	-
HHV-6A	GS <sup>d</sup>	10.2 +/- 1.3	2.7	-	-	-
HHV-6B	Z29 <sup>d</sup>	2.9 +/- 1.1	4.1	-	-	-

ACV = acyclovir, FOS = foscarnet, GCV = ganciclovir, CDV = cidofovir

<sup>a</sup> plaque reduction assay (average +/- SD, n=3 [n=1 when no SD present]) <sup>b</sup> - equals not tested

<sup>c</sup> CPE assay (average +/- SD, n=2 [n=1 when no SD present])

<sup>d</sup> DNA hybridization assay (average +/- SD, n=2),

EC 50 = 50% effective concentration

### *In vivo* effect of dose and time on microbicide activity of REP 2006 (REP 9) against HSV-2 challenge

Group	Drug	Concentration	Time	N	Animals protected	
					against disease	against infection <sup>a</sup>
Experiment 1						
1	REP 9	100 mg/ml	5 min	12	8/12 (67%) <sup>b</sup>	8/12 (67%) <sup>b</sup>
2	PRO 2000	4% GEL	5 min	12	12/12 (100%) <sup>c</sup>	12/12 (100%) <sup>c</sup>
3	PBS	n/a	5 min	12	0/12 (0%)	0/12 (0%)
Experiment 2						
1	REP 9	100 mg/ml	5 min	12	6/12 (50%)	6/12 (50%)
2	REP 9	275 mg/ml	5 min	12	9/12 (75%) <sup>d</sup>	9/12 (75%)
3	REP 9	275 mg/ml	30 min	12	9/12 (75%) <sup>d</sup>	9/12 (75%) <sup>d</sup>
4	PRO 2000	4% GEL	30 min	12	12/12 (100%) <sup>e</sup>	12/12 (100%) <sup>e</sup>
5	PRO 2000	4% GEL	5 min	8	7/8 (88%) <sup>e</sup>	7/8 (88%) <sup>e</sup>
6	PBS		5 min	12	1/12 (8%)	1/12 (8%)

<sup>a</sup> Animals without symptoms were defined as infected if virus was isolated from subject swabs on day 2 after inoculation.

<sup>b</sup> p < 0.001 compared to PBS using Fisher's Exact Test

<sup>c</sup> p < 0.001 compared to PBS using Fisher's Exact Test

<sup>d</sup> p < 0.005 compared to PBS using Fisher's Exact Test

<sup>e</sup> p < 0.001 compared to PBS using Fisher's Exact Test, NS compared to REP 9 at 275 mg/ml

### In vivo effect of REP 2006 (REP 9C) against genital HSV-2 challenge

Experiment 1					Animals protected	
Group	Drug	Concentration	Time	N	against disease	against infection <sup>a</sup>
1	REP 9C	240 mg/ml	5 min	12	9/12 (75%) <sup>b</sup>	9/12 (75%) <sup>b</sup>
2	REP 9C	100 mg/ml	5 min	11	11/11 (100%) <sup>b</sup>	11/11 (100%) <sup>b</sup>
3	PBS	n/a	5 min	12	0/12 (0%)	0/12 (0%)
4	PRO 2000	4% GEL	5 min	7	7/7 (100%)	7/7 (100%)
Experiment 2						
1	REP 9C	240 mg/ml pbs	60 min	12	6/12 (50%) <sup>c</sup>	4/12 (33%)
2	REP 9C	240 mg/ml pbs	30 min	12	10/12 (83%) <sup>b</sup>	8/12 (67%) <sup>d</sup>
3	REP 9C	100 mg/ml pbs	30 min	12	4/12 (33%)	4/12 (33%)
4	REP 9C	100 mg/ml pbs	5 min	12	12/12 (100%) <sup>b</sup>	12/12 (100%) <sup>b</sup>
5	PBS	n/a	5 min	12	1/12 (8%)	1/12 (8%)

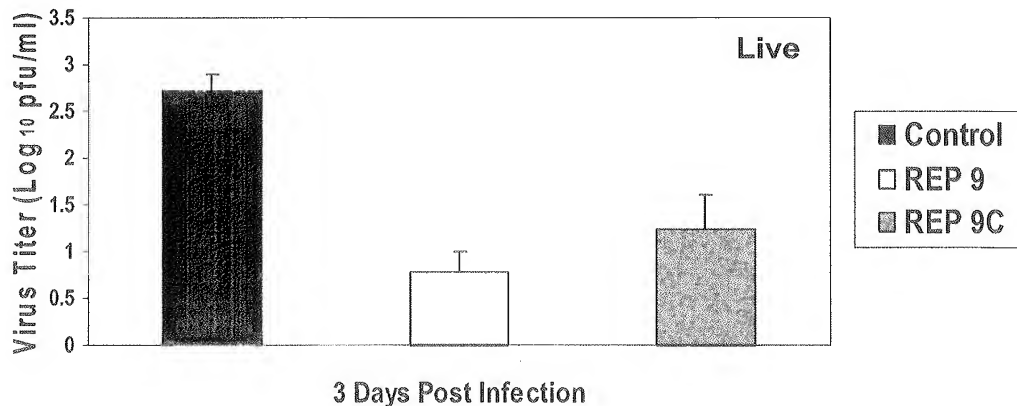
<sup>a</sup> Animals without symptoms were defined as infected if virus was isolated from subject swabs on day 2 after inoculation.

<sup>b</sup>  $p < 0.001$  compared to PBS control (Fischer's exact, two-tailed)

<sup>c</sup>  $p = 0.07$  compared to PBS control

<sup>d</sup>  $p < 0.05$  compared to PBS control

### In vivo Antiviral Activity of REP 2006 (REP 9) and REP 2031 (REP 9C).



Legend: Virus titer levels in the livers from saline-treated control mice (black bar), mice treated with 10 mg/kg REP 9 (white bar), and mice treated with 10 mg/kg REP 9C (gray bar). Mice (8 mice/group) were treated by daily i.p. administration of saline, REP 9, or REP 9C starting 2 days prior to infection with MCMV and continued to 3 days post infection. Tissues were sonicated and titered on NIH3T3 cells. Data represents results from three separate experiments; Mean  $\pm$  standard error (n=8). \* = statistically significant difference for 10 mg/kg REP 9 vs. control, Liver,  $p < 0.0001$ ; \*\* = statistically significant difference for 10 mg/kg REP 9C vs. control, Liver,  $p = 0.002$ . B) Spleen weights of saline-treated control mice (black bar), uninfected mice treated with 10 mg/kg REP 9 (striped bar), mice treated with 10 mg/kg REP 9 (white bar), and mice treated with 10 mg/kg REP 9C (gray bar). Data represents results from one experiment; Mean  $\pm$  standard deviation (n=8).

8. I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by a fine or imprisonment, or both (18 U.S.C. Sec. 1001), and may jeopardize the validity of the application of any patent issuing thereon.

Signed

A handwritten signature in dark ink, appearing to read 'J M Juteau', written in a cursive style.

Jean-Marc Juteau

Dated: June 4th, 2008



## *Curriculum vitae*

### JEAN-MARC JUTEAU, Ph.D

Address: 66 de Vincennes  
Blainville, QC  
Canada  
H7B 1W7

Telephone: (450) 434-8932 (home)  
(450) 688-6068 x2 (work)

Born: 1962

Status: Married, three children

Language spoken and written: French and English

Citizenship: Canadian

### EXPERIENCE

#### 01-2002 - today

**Senior Vice-President and Founder, REPLICor Inc., Laval.**  
Biopharmaceutical company developing antiviral drugs.

##### Responsibilities:

- In charge of intellectual property portfolio.  
*Patent writing, strategy, management.*
- Involved in science development.  
*Day to day contact with CSO, scientific input.*
- In charge of business development.  
*Primary contact with pharmaceutical companies*
- In charge of external contracts.  
*For more than 20 subcontractors.*

#### 02-1999 – 01-2002

**CEO and Founder, REPLICor Inc., Laval.**

##### Responsibilities:

- Involved in science development  
*Co-inventor of REP 9AC technology*
- In charge of financing
- In charge of licensing and contract agreement
- In charge of business development
- Involved in company management
- In charge of R&D tax credit

CONFIDENTIAL

02-1996 to 02-1999

**Officer, Office of Technology Transfer, McGill University, Montreal.**

Responsibilities:

- Agreement management and negotiation  
*License, research, option, confidentiality, material distribution.*
- Spin-off company projects  
*Set-up of spin-off company, contact with investors, business plan.*
- Promotion of technology  
*Technology marketing, contact with the industry.*
- Management of inventions  
*Patent filing, management of report of inventions.*

03-94 to 02-96

**Product Manager, Iso Tech Design, Laval.**

Company developing and marketing micro-environments for pharma applications.

Responsibilities:

- Microbiology quality control.
- Distributor formation  
*Contacts: Baxter Health Care, VWR, Khulman Tech., E.S.I. FluFrance, Liberty Clean Rooms, Millipore.*
- Development of selling aides  
*Data sheet, promotional video, publicity.*
- Sales  
*Clients: Hospital pharmacy, research, pharmaceutical industry. Canada and US*
- Commercial meeting organization  
*Canada and US*
- Internal market study
- R&D.

01-94 à 06-94

**Part time columnist for CKAC radio-73.**

Highest rating Montreal AM radio

Responsibilities: Weekly scientific column

91 à 10-93

**Director and co-founder, DIAGNOGENE inc., R&D in biotechnology, Ste-Foy.**

Company developing molecular detection tools for environmental pathogens.

Responsibilities: Financial and research administration, representation.

## **RESEARCH TRAINING**

09-92 à 11-93

**Post-doctoral scientist, INRS-santé, Pointe-Claire.**

Project: In-vitro mutagenesis of 4-chlorobenzoate dehalogenase in *Pseudomonas sp.* CBS3.

08-91 à 09-92

**Post-doctoral scientist, Institut de Recherches Cliniques de Montréal.**

Project: Cloning and characterization of cardiac specific transcription factors.

11-90

Training in molecular modeling, Department of Molecular and Cell Biology, **U. Connecticut.**

06-88

Workshop on DNA technologies: Sequence and in-vitro mutagenesis, **U. North-Carolina**, Chapel Hill, NC.

**CONFIDENTIAL**

## EDUCATION

87-91

**Doctorate** (Ph.D.), Microbiology and Immunology, **Laval University**.

Project: Molecular biology, epidemiology and structure-function analysis of the ROB-1  $\beta$ -lactamase.

85-87

**Master** (M.Sc.), Microbiology and Immunology, **University of Montreal (U. of M. Hospital Center)**.

Project: Granulocytar function in recurrent vaginitis.

82-85

**Bachelor** (B.Sc.), Biology, **University of Montreal**.

## SCHOLARSHIP

Institut National de la Recherche Scientifique (INRS) Fellowship, 1992-93.

Medical Research Council (MRC) Fellowship, 1992.

Fonds de la Recherche en Santé du Québec (FRSQ) Studentship, 1989-90-91.

Fonds pour la Formation des Chercheurs et l'Aide à la Recherche (FCAR) Studentship, 1988-89.

## BOARD MEMBERSHIP

2004- today

President of the Alumni Association of Montreal Clinical Research Institute.

2005- 2007

Member of the Montreal Life Science Committee.

2003- 2005

Member of the Board of BioQuebec (Québec Association of Biotechnology Companies)

## AWARD and PRIZES

Finalist, Canada's Top 10 Life Science Companies Competition 2007 (to REPLICor)

Finalist, Canada's Top 10 Life Science Companies Competition 2004 (to REPLICor)

DEKA Award 2000 High Technology, Hellenic Board of Trade of Montreal (to REPLICor)

Industrial Design Prize 1995 from the Design Institute (received in team for a micro-environment)

Canlab Prize from Association des Microbiologistes du Québec, 1989.

CONFIDENTIAL

David I Bernstein, Nathalie Goyette, Rhonda Cardin, Earl R. Kern, Guy Boivin, James Ireland Jean-Marc Juteau, Andrew Vaillant. Amphipathic DNA Polymers Exhibit Anti-herpetic Activity In vitro and In vivo. *Antimicrob Agents Chemother*. 2008 May 27. [Epub ahead of print].

Esmeralda M. Guzman, Natalia Cheshenko, Vikas Shende, Marla J. Keller, Nathalie Goyette, Jean-Marc Juteau, Guy Boivin, Andrew Vaillant (co-corresponding author), and Betsy C. Herold. 2007. Amphipathic DNA Polymers Prevent HSV Infection and Block Multiple Steps in Viral Life Cycle. *Antiviral Therapy* 12: 1147-1156.

Andrew M Lee, Jillian M Rojek, Anette T Gundersen, Ute Stroeher, Jean-Marc Juteau, Andrew Vaillant, Stefan Kunz. 2007. Inhibition of Cellular Entry of Lymphocytic Choriomeningitis Virus by Amphipathic DNA Polymers. *Virology* 372: 107-117.

Andrew Vaillant, David A. Kocisko, Kil Sun Lee, Kevin M. Arnold, Nadine Bertholet, Richard E. Race, Emily A. Olsen, Jean-Marc Juteau (co-corresponding author) and Byron Caughey. 2006. Potent Antiscrapie Activities of Degenerate Phosphorothioate Oligonucleotides. *Antimicrobial Agents and Chemotherapy*. 50: 1034-1044

Andrew Vaillant (co-corresponding author), Jean-Marc Juteau, Hong Lu, Shuwen Liu, Carol Lackman-Smith, Roger Ptak, and Shibo Jiang. 2006. Phosphorothioate Oligonucleotides Inhibit Human Immunodeficiency Virus Type 1 Fusion by Blocking gp41 Core Formation. *Antimicrobial Agents and Chemotherapy*. 50: 1393-1401

The synthesis and initial characterization of an immobilized DNA unwinding element binding (DUE-B) protein chromatographic stationary phase. Ruin Moaddel, Gerry B. Price, Jean-Marc Juteau, Michael Leffak and Irving W. Wainer. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2005 Jun 25;820(2):197-203.

Sylvestre M, Sirois M, Hurtubise Y, Bergeron J, Ahmad D, Shareck F, Barriault D, Guillemette I, Juteau JM. Sequencing of *Comamonas testosteroni* strain B-356-biphenyl/chlorobiphenyl dioxygenase genes: evolutionary relationships among Gram-negative bacterial biphenyl dioxygenases. *Gene*. 1996 Oct 3;174(2):195-202.

Ahmad D, Fraser J, Sylvestre M, Larose A, Khan A, Bergeron J, Juteau JM, Sondossi M. Sequence of the bphD gene encoding 2-hydroxy-6-oxo-(phenyl/chlorophenyl)hexa-2,4-dienoic acid (HOP/cPDA) hydrolase involved in the biphenyl/polychlorinated biphenyl degradation pathway in *Comamonas testosteroni*: evidence suggesting involvement of Ser112 in catalytic activity. *Gene*. 1995 Apr 14;156(1):69-74.

Juteau JM, Billings E, Knox JR, Levesque RC. Site-saturation mutagenesis and three-dimensional modelling of ROB-1 define a substrate binding role of Ser130 in class A beta-lactamases. *Protein Eng*. 1992 Oct;5(7):693-701.

Maclean IW, Slaney L, Juteau JM, Levesque RC, Albritton WL, Ronald AR. Identification of a ROB-1 beta-lactamase in *Haemophilus ducreyi*. *Antimicrob Agents Chemother*. 1992 Feb;36(2):467-9.

Juteau JM, Cote S, Levesque RC. Systematic site-saturation mutagenesis of ROB-1 beta-lactamase: efficiency of T4 polymerase and oligonucleotide synthesis. *Biotechniques*. 1991 Oct;11(4):460-2. No

Juteau JM, Sirois M, Medeiros AA, Levesque RC. Molecular distribution of ROB-1 beta-lactamase in *Actinobacillus pleuropneumoniae*. *Antimicrob Agents Chemother*. 1991 Jul;35(7):1397-402.

Juteau JM, Levesque RC. Sequence analysis and evolutionary perspectives of ROB-1 beta-lactamase. *Antimicrob Agents Chemother*. 1990 Jul;34(7):1354-9.

#### *Public Presentations (2005 - today)*

Faseeha Noordeen, Andrew Vaillant, Jean-Marc Juteau, and Allison Jilbert. Amphipathic DNA polymers inhibit duck hepatitis B virus infection in vitro. Presented at the International Meeting on the Molecular Biology of Hepatitis B Viruses, Rome Italy 2007

CONFIDENTIAL

Faseeha Noordeen, Andrew Vaillant, Jean-Marc Juteau, and Allison Jilbert. Amphipathic DNA polymers inhibit duck hepatitis B virus infection in vivo. Presented at the International Meeting on the Molecular Biology of Hepatitis B Viruses, Rome Italy 2007

Takuya Matsumura, Takanobu Kato, Zongyi Hu, Jean-Marc Juteau, Andrew Vaillant, T. Jake Liang. A novel class of amphipathic DNA polymers inhibits hepatitis C virus infection by blocking viral entry. Presented at the RSC / Virus Molecular Interactions Conference, Oxford, UK September 2007

Andrew Vaillant, Jean-Marc Juteau, Annie Lebel, Nathalie Goyette, Guy Boivin, Phil Wyde. Mechanism of action of Phosphorothioate oligonucleotides Against Influenza virus. Presented at the Meeting of the American Society for Microbiology, Orlando, Florida, May, 2006

Takuya Matsumura, Takanobu Kato, Zongyi Hu, Jean-Marc Juteau, Andrew Vaillant, T. Jake Liang. A Novel Class of Amphipathic DNA Polymers Inhibits Hepatitis C Virus Infection by Blocking Viral Entry. Presented at the Annual meeting of the AASLD, November 2006.

Andrew Vaillant, Charles Lavigne, Nadine Bertholet, Jean-Marc Juteau and André Marette. REP 9C prevents the development of obesity and dyslipidemia induced by a high fructose diet in hamsters. Presented at the NAASO meeting, Boston, Mass, October 2006

Andrew Vaillant, Annie Lebel, Nathalie Goyette, Guy Boivin, Jean-Marc Juteau Phil Wyde. REP 9: A potent Broad Spectrum Aerosol Prophylaxis and Therapy Against Influenza Infection In Vivo. Presented at the 4<sup>th</sup> International Conference on Influenza. London, UK, June 2006

Shailja Singh, Andrew Vaillant, Ahmed Rushdi Shakri, Syed Shams Yazdani, Michel Bazinet, Jean-Marc Juteau, Chetan E. Chitnis. Potent inhibition of erythrocyte invasion by malaria parasites using degenerate phosphorothioate oligonucleotides. Presented at the Keystone Symposium on Malaria, Taos, New Mexico, March 2006.

David A. Kocisko, Andrew Vaillant, Kil Sun Lee, Kevin M. Arnold, Nadine Bertholet, Richard E. Race, Emily A. Olsen, Jean-Marc Juteau, Byron Caughey. Potent In Vitro Anti-Scrapie Activities of Degenerate Phosphorothioate Oligonucleotides. Presented at the 1<sup>st</sup> Annual Meeting of the Oligonucleotide Therapeutics Society Meeting, New York, NY, September 2005

Andrew Vaillant, Hong Lu, Shuwen Liu, Carol Lackman-Smith, Roger Ptak, Jean-Marc Juteau and Shibo Jiang Phosphorothioate Oligonucleotides Inhibit HIV-1 Fusion in a Sequence Independent Manner by Blocking GP41 Core Formation. Presented at the 1<sup>st</sup> Annual Meeting of the Oligonucleotide Therapeutics Society Meeting, New York, NY, September 2005

Andrew Vaillant, Louis Flamand, Nathalie Goyette, James Ireland, Annie Lebel, Earl Kern, Guy Boivin, Rhonda Cardin, David Bernstein, Jean-Marc Juteau. Sequence Independent Antiviral Activity of Phosphorothioate Oligonucleotides Against Herpesviridae In Vivo By Topical and Systemic Administration. Presented at the 1<sup>st</sup> Annual Meeting of the Oligonucleotide Therapeutics Society Meeting, New York, NY, September 2005

Andrew Vaillant, John Casper, Michael Leffak, Jean-Marc Juteau Antisense-based Attenuation of DUE-B Expression Has Potent Anti-Proliferative Activity. Presented at the 1<sup>st</sup> Annual Meeting of the Oligonucleotide Therapeutics Society Meeting, New York, NY, September 2005

Andrew Vaillant, Ute Ströher, David Evans, Steven Jones, Heinz Feldmann, Jean-Marc Juteau SSequence-Independent Antiviral Activity of Phosphorothioate Oligonucleotides Against Biodefence-Relates Viruses. Presented at the 1<sup>st</sup> Annual Meeting of the Oligonucleotide Therapeutics Society Meeting, New York, NY, September 2005

Andrew Vaillant, Annie Lebel, Nathalie Goyette, Guy Boivin, Jean-Marc Juteau, Phil Wyde Aerosolized Phosphorothioate Oligonucleotides Have Sequence-Independent Antiviral Activity In Vivo Against Influenza and RSV. Presented at the 1<sup>st</sup> Annual Meeting of the Oligonucleotide Therapeutics Society Meeting, New York, NY, September 2005

Vaillant, A., Flamand, L., Goyette, N., Ireland, J., Lebel, A., Kern, E., Boivin, G., Bernstein, D. and Juteau, JM. Degenerate Phosphorothioate Oligodeoxynucleotides are a Potent Antiviral Agent for Herpesviruses. Presented at the 18th International Conference on Antiviral Research, Barcelona, Spain April, 2005.

Vaillant, A., Wyde, P., Lebel, A., Goyette, N., Boivin, G. and Juteau, JM. Degenerate Phosphorothioate Oligodeoxynucleotides are a Potent Antiviral Agent for Influenza Viruses. Presented at the 18th International Conference on Antiviral Research, Barcelona, Spain, April, 2005.

Ströher, U., Vaillant, A., Juteau, JM, Jones, S. and Feldmann, H. Degenerate Phosphorothioate Oligodeoxynucleotides are a Potent Antiviral Agent for Filoviruses and Arenaviruses. Presented at the 18th International Conference on Antiviral Research, Barcelona, Spain, April, 2005.